UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,265	08/31/2001	Timothy A. Springer	CBN-002CP	1985

28120 7590 02/14/2006

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/945,265	SPRINGER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77,80,84,87,88,105,106,114,115,128,133 and 134* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of the pervious Office action mailed 9/22/05 is hereby withdrawn, a new ground of rejection is set forth herein.

2. Claims 77, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 are pending and under examination in the instant application.

3. The specification stands objected to for the following discrepancies: the specification on page 28 discloses that the αL K287C/K294C mutant is a modified αL polypeptide, wherein there is a change in the amino acid sequence of al (SEQ ID NO:2) such that amino acid residues 287 and 294 are substituted with cysteine residues. The corresponding wild wild-type nucleotide sequence, SEQ ID NO:1, is modified at nucleotide residues 1022-1024 and 1143-1145, respectively. However, there is no corresponding amino acids at positions 284, 287, 289, 294, 301 of SEQ ID NO: 2. The amino acid at positions positions 284, 287, 289, 294, 301 of SEQ ID NO: 2 are I (Ile), G (Gly), H (His), E (Glu) and K (lys), respectively. Further table 9, discloses several mutation in the αL that do not correspond to the amino acid number in SEQ ID NO:2. Corrections/clarifications are required.

Further, there are discrepancies between table 9, col. 4, row 4, wherein the αL K294 nucleotide mutant is 1043-1045 while the specification on page 28, line 9 discloses that the same mutant is at 1143-1145.

Applicant is required to check all the disclosed amino/nucleic acid mutation positions to make sure they are correspondent with the referenced SEQ ID NO.

The Declaration of Dr. Shimaoka under 37 C.F.R 1.132 filed 1/23/06 is insufficient to overcome the objection to the specification because the Declaration Dr. Shimaoka refers to published sequences to distinguish between the disclosed mature LFA-1 of SEQ ID NO: 2 (lacks 25 amino acids) and the used LFA-1 in the specification is based on published precursor LFA-1, however the examiner could not find those published sequences. Further, the specification still refers to SEQ ID NO: 2 for the particular mutations. Finally, the Examiner notes that page 28, line 13, refers to αL: GenBanK NM_002209 sequence, however said sequence is the same as disclosed SEQ ID NO:2.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

5. Claims 77, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 84, 87, 88, 133 and 134 are indefinite and ambiguous in the recitation of "E284C/E301C", "K287C/K294C" and K289C/K294C" in claims 84, 87, 88 and 133-134. Recitation of amino acid position without providing SEQ ID NO for the polypeptide is indefinite and ambiguous because different laboratories may have different numbering of the same polypeptide. It is indefinite to refer to amino acid position without structural features the integrin I-domain of an αL integrin.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 77, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide **enablement** for an antibody, or antigen bidnig fragment therof, which binds to "any integrin I-domain" of "any αL integrin", the-I-domain being locked in the open conformation by the substitutions E284C/E301C or K287C/K294C but not to a modified integrin I-domain that is locked in the closed conformation by the substitutions K289C/K294C in claim 84, wherein the I-domain in the open conformation comprises substitutions E284C/E301C in an αL subunit in claim 87, wherein the I-domain in the open conformation comprises substitutions K287C/K294C in an αL subunit in claim 88, or a recombinant antibody, or an antigen binding fragment thereof, which binds to "any integrin I-domain" of "any αL integrin", the I-domain being locked in the open conformation by the substitutions E284C/E301C but not to "any modified αL integrin I-domain" that is locked in the closed conformation by the substitutions K289C/K294C, wherein the antibody or antigen binding fragment thereof blocks interaction between LFA-1 and ICAM-1 in claim 133 or a recombinant antibody, or an antigen binding fragment thereof, which binds to "any integrin I-domain" of "any αL integrin", the I-domain being locked in the open conformation by the substitutions K287C/K294C but not to "any modified αL integrin I-domain" that is locked in the closed conformation by the substitutions K289C/K294C, wherein the antibody or antigen binding fragment thereof blocks interaction between LFA-1 and ICAM-1 in claim 134. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Besides the human αL polypeptide of SEQ ID NO: 2, the specification fails to establish the structure of αL integrin to which the claimed antibody binds (see page 28, lines 5-9). "αL integrin" is an arbitrary protein name. The scope of the claims is not commensurate with the

enablement provided by the disclosure with regard to the extremely large number of αL integrin polypeptides (human, mouse, rat, mature, precursor, among other species) broadly encompassed by the claims.

While the specification provides the human αL polypeptide of SEQ ID NO: 2, the recited substitutions E284C/E301C, K287C/K294C and K289C/K294C do not correspond to the amino acids of the human αL polypeptide of SEQ ID NO: 2. The skilled in the art would not know how to make such substations when there are no correspondent amino acids in the αL integrin and hence would not know how to make the claimed antibody.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 77, 80, 84, 87-88, 105-106, 114-115, 128 and 133-134 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of an antibody, or antigen bidnig fragment therof, which binds to "any integrin I-domain" of "any αL integrin", the-I-domain being locked in the open conformation by the substitutions E284C/E301C or K287C/K294C but not to a modified integrin I-domain that is locked in the closed conformation by the substitutions K289C/K294C in claim 84, wherein the I-domain in the open conformation comprises substitutions E284C/E301C in an αL subunit in claim 87, wherein the I-domain in the open conformation comprises substitutions K287C/K294C in an αL subunit in claim 88, or a recombinant antibody, or an antigen binding fragment thereof, which binds to "any integrin I-domain" of "any αL integrin", the I-domain being locked in the open conformation by the substitutions E284C/E301C but not to "any modified αL integrin I-domain" that is locked in the closed conformation by the substitutions K289C/K294C, wherein the antibody or antigen binding fragment thereof blocks interaction between LFA-1 and ICAM-1 in claim 133 or a recombinant antibody, or an antigen binding fragment thereof, which binds to "any integrin I-domain" of "any αL integrin", the I-domain being locked in the open conformation by the substitutions K287C/K294C but not to "any modified αL integrin I-domain" that is locked in the closed conformation by the substitutions K289C/K294C, wherein the antibody or antigen binding fragment thereof blocks interaction between LFA-1 and ICAM-1 in claim 134.

Applicant has disclosed only amino acid of SEQ ID NO: 2; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The

Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

February 9, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600